Small and shallow optic cup morphology is associated with optic disc edema development during spaceflight

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Introduction

Approximately 70% of crewmembers completing long-duration (4 – 6 month) spaceflight missions develop signs of optic disc edema (ODE), a finding of spaceflight-associated neuro-ocular syndrome (SANS, **Fig. 1**). The onset and magnitude of spaceflight-induced ODE differs across individuals.[1,2] Identifying factors that explain this variability is of high priority because of documented SANS cases involving substantial ODE and because ODE may be more severe during missions of >1 year. Considering terrestrial diseases involving ODE,[3] we tested whether having crowded optic nerve head (ONH) morphology prior to flight increases susceptibility to spaceflight-induced ODE. We also evaluated body weight, which has been previously linked to ODE and choroidal folds after spaceflight.[4]

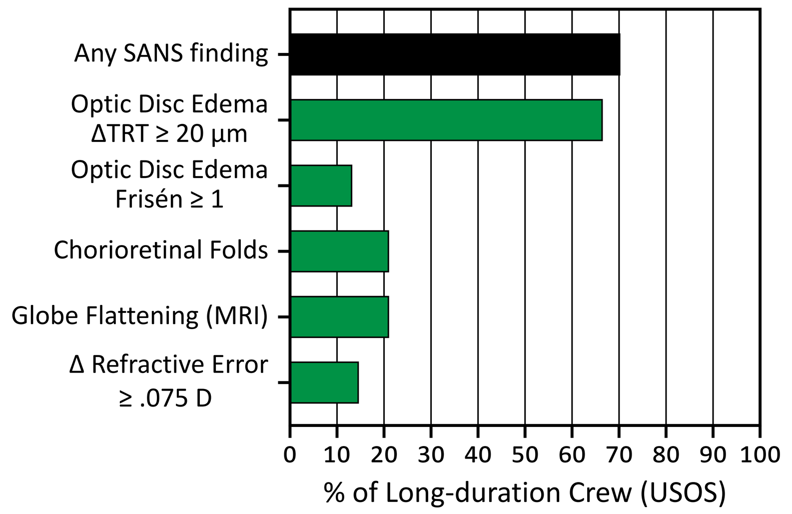


Figure 1. Most long-duration crewmembers present at least one sign of SANS (i.e., ODE development, chorioretinal folds, globe flattening, hyperopic shifts in refractive error). Nearly all cases include ODE development according to objective optical coherence tomography (OCT)-based measurement of peripapillary total retinal thickness (TRT), even if not ≥1 on the Frisén grading scale.

Methods

Radial and circular OCT scans centered on the ONH were collected preflight and on flight day ~150 from both eyes of 31 crewmembers. ONH morphology was quantified (**Fig. 2**), as were retinal nerve fiber layer thickness and choroid thickness. Axial length, cycloplegic refractive error, and body weight and height data were requested from NASA's Life Sciences Data Archive. Associations between preflight variables and inflight peripapillary TRT changes were assessed using a linear mixed-effects model. Within each variable, inflight and postflight values were compared to preflight (**Table**).

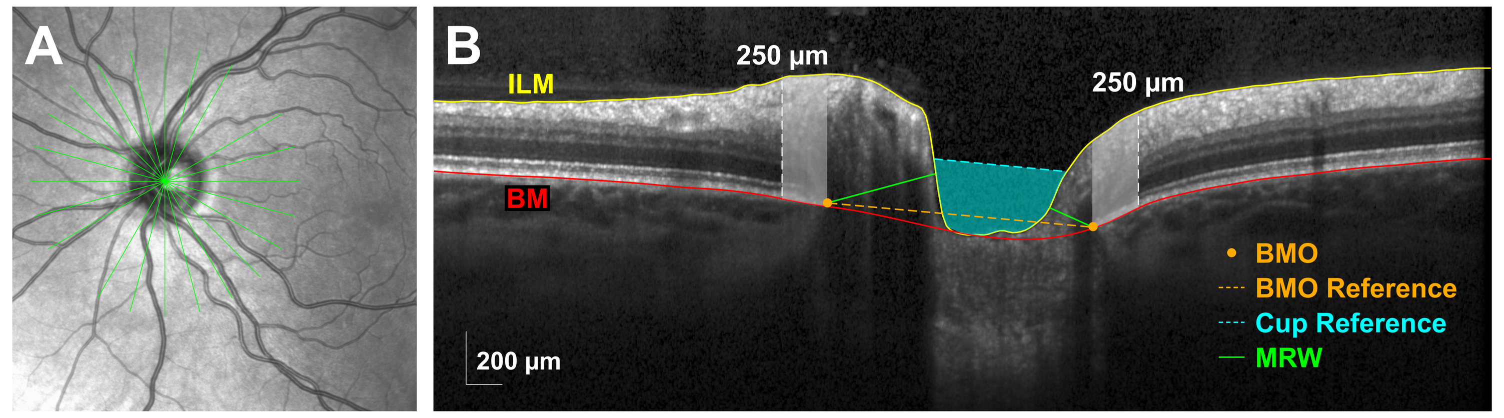


Figure 2. Evaluation of ONH morphology. **A)** 30° infrared image with radial scan pattern. **B)** OCT B-scan with segmentations of the internal limiting membrane (ILM, yellow) and Bruch's membrane (BM, red), BM opening (BMO) points (orange dots), BMO reference (orange dashed line), cup reference (cyan dashed line) located 200 µm anterior to the BMO reference, minimum rim width (MRW, green), and 250 µm annulus extending from BMO (gray shaded region) used to quantify TRT.[5] The optic cup is shaded (cyan).

Results

Optic disc edema development is observed across both sexes and eyes at flight day ~150

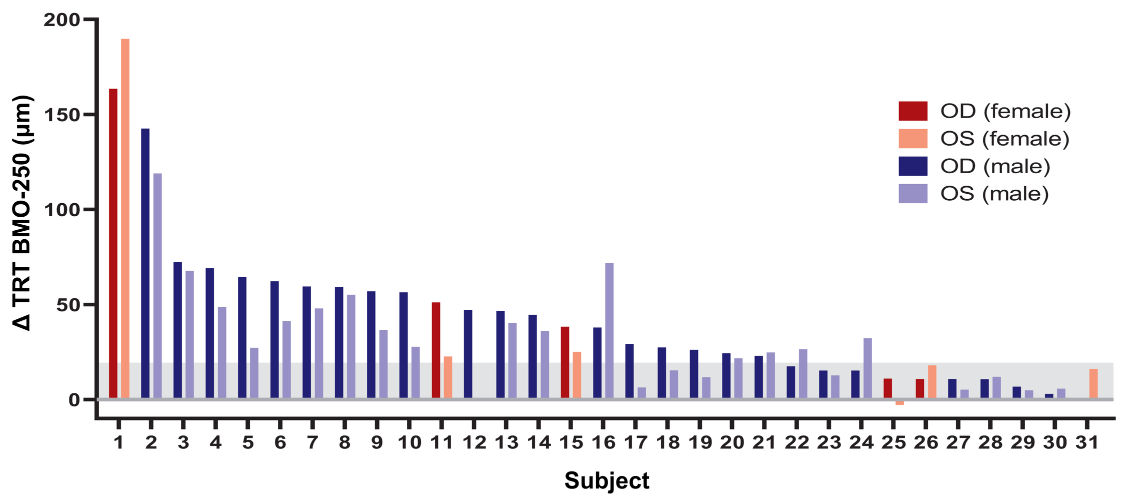


Figure 3. Increases in TRT above the predefined 20 µm threshold for ODE development (gray). Female, red; male, blue; OD, right eye, dark color; OS, left eye, light color.

A smaller optic cup is associated with optic disc edema development during spaceflight

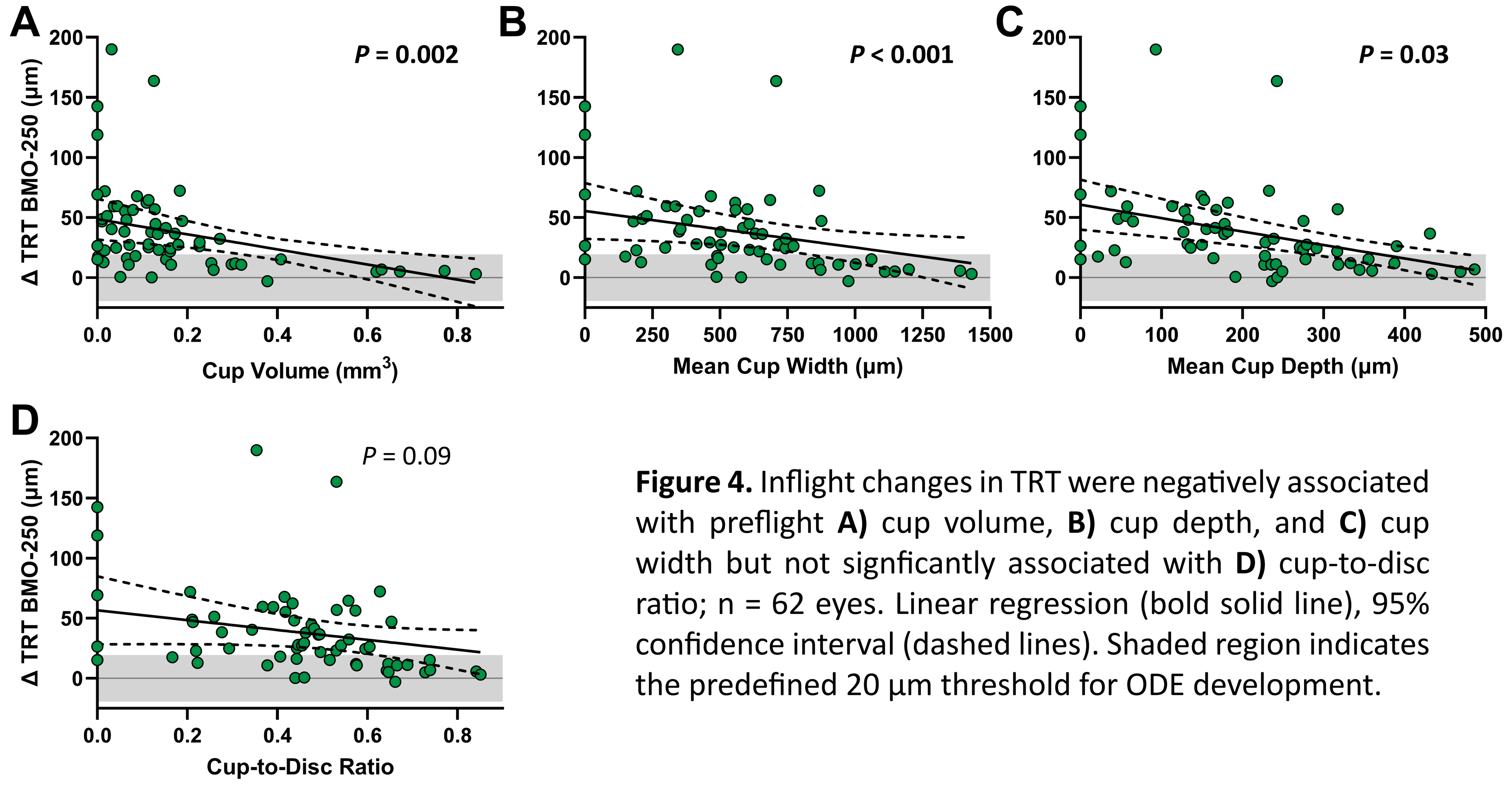
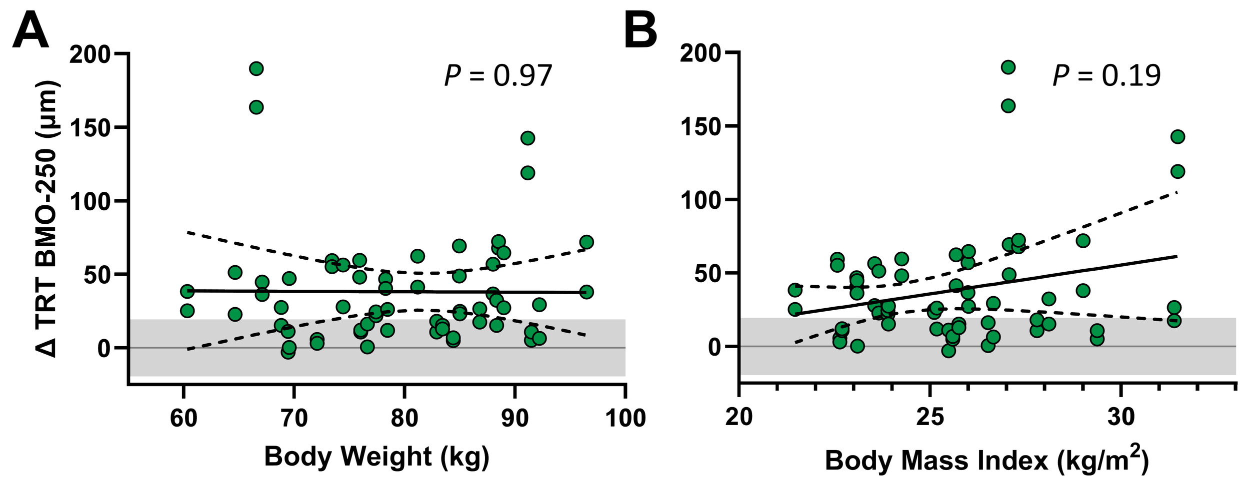


Figure 4. Inflight changes in TRT were negatively associated with preflight **A)** cup volume, **B)** cup depth, and **C)** cup width but not signficantly associated with **D)** cup-to-disc ratio; n = 62 eyes. Linear regression (bold solid line), 95% confidence interval (dashed lines). Shaded region indicates the predefined 20 µm threshold for ODE development.

Preflight values for cup-to-disc ratio, TRT, MRW, BMO area, RNFL thickness, choroid thickness, axial length, and refractive error were not associated with ODE development.

Body weight is not associated with ODE development during spaceflight

Figure 5. Inflight changes in TRT were not associated with preflight **A)** body weight or **B)** body mass index (BMI); n = 62 eyes. Linear regression (bold solid line), 95% confidence interval (dashed lines). Shaded region indicates the predefined 20 µm threshold for ODE development.



Ocular characteristics of the cohort

	Preflight		Inflight			Postflight		
	Mean ± SE	Range	Mean ± SE	Range	P-value	Mean ± SE	Range	P-value
TRT BMO-250 (µm)	392.0 ± 5.8	(299.3, 483.9)	430.2 ± 9.6	(305.1, 593.4)	<0.001	419.3 ± 7.9	(303.3, 541.4)	<0.001
Minimum rim width (µm)	366.4 ± 9.1	(225.1, 493.8)	416.3 ± 12.6	(237.8, 572.4)	<0.001	400.8 ± 11.4	(230.5, 532.2)	<0.001
Cup volume (mm^3)	0.167 ± 0.033	(0, 0.841)	0.134 ± 0.033	(0, 0.787)	<0.001	0.146 ± 0.034	(0, 0.840)	<0.001
Mean cup depth (µm)	201.2 ± 21.5	(0, 486.3)	178.0 ± 23.5	(0, 472.5)	0.001	189.0 ± 22.6	(0, 493.8)	0.007
Mean cup width (µm)	570.0 ± 57.3	(0, 1431.5)	480.0 ± 62.7	(0, 1443.0)	<0.001	513.0 ± 61.0	(0,1447.7)	<0.001
Cup-to-disc ratio	0.45 ± 0.03	(0.38, 0.52)	0.37 ± 0.04	(0.30, 0.45)	<0.001	0.40 ± 0.04	(0.33, 0.48)	<0.001
BMO area (mm2)	2.02 ± 0.07	(1.33, 4.11)	2.06 ± 0.08	(1.35, 4.18)	0.003	2.04 ± 0.08	(1.33, 4.14)	0.13
RNFL thickness (µm)	104.0 ± 1.6	(83.3, 126.1)	106.7 ± 1.7	(83.5, 133.1)	0.002	106.3 ± 1.5	(84.6, 124.7)	<0.001
Choroid thickness (µm)	213.3 ± 11.1	(107.0, 406.4)	245.6 ± 11.9	(134.4, 488.5)	<0.001	229.0 ± 11.5	(118.5, 466.2)	<0.001
Axial length (mm)	24.1 ± 0.17	(22.0, 25.8)	N/A	N/A	N/A	23.9 ± 0.16	(21.9, 25.6)	<0.001
Refractive Error (D)	-0.41 ± 0.21	(-3.25, 1.75)	N/A	N/A	N/A	-0.21 ± 0.20	(-3.25, 2.25)	0.02

Table. Inflight, flight day ~150; Postflight, within 1 week of landing. Refractive error is the spherical equivalent cycloplegic refraction. P-values for inflight and postflight measurements describe comparisons to preflight measurements. SE, standard error.

Conclusions

- Preflight optic cup size may explain individual variability in spaceflight-induced ODE onset and magnitude. The other ocular parameters evaluated do not share this association, nor do preflight body weight or BMI.
- Crewmembers with relatively small optic cups, preflight, could have an increased risk of developing ODE, so they may therefore benefit from additional ophthalmic monitoring during spaceflight and from SANS countermeasures.
- The association between optic cup size and ODE development may be informative for extended duration missions to the Moon and Mars.

References

1. Macias BR, Patel NB, Gibson CR, *et al*. (2020). Association of long-duration spaceflight with anterior and posterior ocular structure changes in astronauts and their recovery. *JAMA Ophthal.*, 138(5):553-559.
2. Mader TH, Gibson CR, Pass AF, *et al*. (2011). Optic disc edema, globe flattening, choriodal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Ophthalmology*, 118, 2058–2069.
3. Hamill E, Kim JD, Yalamanchili S, *et al*. (2014). Cup-to-disc ratio in idiopathic intracranial hypertension without papilloedema. *Neuroophthalmology*, 38(2):69-73.
4. Buckey JC, Phillips SD, Anderson AP, *et al*. (2018) Microgravity-induced ocular changes are related to body weight. *Am J Physiol Regul Integr Comp Physiol*. 315(3):R496-R499.
5. Patel N, Pass A, Mason S, et al. (2018) Optical Coherence Tomography Analysis of the Optic Nerve Head and Surrounding Structures in Long-Duration International Space Station Astronauts. *JAMA Ophthal.*, 136(2):193-200.

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